

In the Claims

1-49 (cancel).

50 (new). A composition of matter comprising:

- a) an isolated polypeptide presenting at least one activity of human IFN γ , and comprising a sequence having at least 80% of homology with the complete sequence of pIFNFHcon (SEQ ID NO: 156) and no more than nine non-conservative mutations in the positions corresponding to Ala10, Gly12, Arg26, Ala31, Lys35, Phe47, Gln55, Glu57, Lys63, and Ile75 in pIFNFHcon;
- b) an isolated polypeptide that comprises a sequence having at least 80% of homology with the complete sequence of pIFNFHcon and no non-conservative mutations in the positions corresponding to Ala10, Gly12, Arg26, Ala31, Lys35, Phe47, Gln55, Glu57, Lys63, and Ile75 in pIFNFHcon;
- c) an isolated sequence chosen from pIFNFH15 (SEQ ID NO: 20), pIFNFH32 (SEQ ID NO: 32), and pIFNFH37 (SEQ ID NO: 36);
- d) an isolated polypeptide that comprises a sequence having at least 80% of homology with the complete sequence of pIFNFHcon and one or two non-conservative mutations in the positions corresponding to Ala10, Gly12, Arg26, Ala31, Lys35, Phe47, Gln55, Glu57, Lys63, and Ile75 in pIFNFHcon;
- e) an isolated polypeptide as set forth in d) that comprises a sequence chosen from pIFNFH04 (SEQ ID NO: 6), pIFNFH03 (SEQ ID NO: 4), pIFNFH08 (SEQ ID NO: 8), pIFNFH20 (SEQ ID NO: 22), pIFNFH23 (SEQ ID NO: 24), pIFNFH12 (SEQ ID NO: 14), pIFNFH25 (SEQ ID NO: 26), pIFNFH13 (SEQ ID NO: 16), pIFNFH14 (SEQ ID NO: 18), pIFNFH36 (SEQ ID NO: 34), and pIFNFH39 (SEQ ID NO: 38);
- f) an isolated polypeptide that comprises a sequence having at least 80% of homology with the complete sequence of pIFNFHcon and three, four, or five non-conservative mutations in the positions corresponding to Ala10, Gly12, Arg26, Ala31, Lys35, Phe47, Gln55, Glu57, Lys63, and Ile75 in pIFNFHcon;

- g) an isolated polypeptide as set forth in f) that comprises a sequence chosen from pIFNFH11 (SEQ ID NO: 12), pIFNFH27 (SEQ ID NO: 28), pIFNFH01 (SEQ ID NO: 2), pIFNFH31 (SEQ ID NO: 30), pIFNFH10 (SEQ ID NO: 10), and pIFNFH42 (SEQ ID NO: 40);
- h) an isolated polypeptide that is a variant, a mature form, or an active fragment of the amino acid sequences SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, and 40;
- i) an isolated polypeptide that is a naturally occurring allelic variant of the sequences SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, and 40;
- j) an isolated polypeptide as set forth in i), wherein the variant is the translation of one or more single nucleotide polymorphisms;
- k) a fusion protein comprising a polypeptide according any one of (a) through (j) and a sequence heterologous to pIFNFHcon;
- l) a ligand binding specifically to a polypeptide according to any one of (a) through (j);
- m) a polypeptide as set forth in any one of a) through l), wherein said polypeptides are in the form of active fractions, precursors, salts, or derivatives;
- n) a polypeptide as set forth in (a) through (l), wherein said polypeptides are in the form of active conjugates or complexes with a molecule chosen from radioactive labels, fluorescent labels, biotin, or cytotoxic agents;
- o) a peptide mimetic designed on the sequence and/or the structure of a polypeptide as set forth in (a);
- p) an isolated nucleic acid encoding for an isolated polypeptide as set forth in any one of (a) through (k);
- q) an isolated nucleic acid comprising the coding portion of a sequence selected from the group consisting of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, and 39, or the complement of said sequence;
- r) a purified nucleic acid which hybridizes under high stringency conditions with a nucleic acid selected from the group consisting of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13,

- 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, and 39, or a complement of said nucleic acid;
- s) a vector comprising a nucleic acid encoding for an isolated polypeptide as set forth in any one of (a) through (k); comprising the coding portion of a sequence selected from the group consisting of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, and 39, or the complement of said sequence; or comprising a nucleic acid which hybridizes under high stringency conditions with a nucleic acid selected from the group consisting of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, and 39, or a complement of said nucleic acid;
 - t) a vector comprising a nucleic acid encoding for an isolated polypeptide as set forth in any one of (a) through (k); comprising the coding portion of a sequence selected from the group consisting of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, and 39, or the complement of said sequence; or comprising a nucleic acid which hybridizes under high stringency conditions with a nucleic acid selected from the group consisting of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, and 39, or a complement of said nucleic acid;
 - u) a vector comprising a nucleic acid encoding for an isolated polypeptide as set forth in any one of (a) through (k); comprising the coding portion of a sequence selected from the group consisting of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, and 39, or the complement of said sequence; or comprising a nucleic acid which hybridizes under high stringency conditions with a nucleic acid selected from the group consisting of SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, and 39, or a complement of said nucleic acid, wherein said nucleic acid molecule is operatively linked to expression control sequences allowing expression in prokaryotic or eukaryotic host cells of the encoded polypeptide;
 - v) a host cell transformed with a vector or a nucleic acid according to any one of (p), (q), (r), (s), (t), or (u);

- w) a transgenic animal cell that has been transformed with a vector or a nucleic acid according to any one of (p), (q), (r), (s), (t), or (u) and having enhanced or reduced expression levels of a polypeptide;
- x) a transgenic non-human organism that has been transformed to have enhanced or reduced expression levels of a polypeptide according to any one of (a) through (j);
- y) a compound that enhances the expression level of a polypeptide a polypeptide according to any one of (a) through (j) in a cell or in an animal; or
- z) a compound that reduces the expression level of a polypeptide according to any one of (a) through (j) in a cell or in an animal.

51 (new). The composition of matter according to claim 50, wherein said fusion protein comprises one or more amino acid sequence belonging a protein sequences selected from: membrane-bound protein, immunoglobulin constant region, multimerization domains, extracellular proteins, signal peptide-containing proteins, or export signal-containing proteins.

52 (new). The composition of matter according to claim 50, wherein said ligand antagonizes or inhibits the IFN γ -related activity of said polypeptide.

53 (new). The composition of matter according to claim 52, wherein said ligand is a monoclonal antibody, a polyclonal antibody, a humanized antibody, or an antigen binding fragment thereof.

54 (new). The composition of matter according to claim 52, wherein said ligand corresponds to the extracellular domain of a membrane-bound protein.

55 (new). The composition of matter according to claim 50, wherein said composition of matter further comprises a pharmaceutically acceptable carrier.

56 (new). The composition of matter according to claim 50, wherein said compound that

enhances the expression level of a polypeptide a polypeptide according to any one of (a) though (j) is an antisense oligonucleotide or a small interfering RNA

57 (new). A method of using the composition of matter for producing cells capable of expressing a polypeptide; for making a polypeptide; the preparation of pharmaceutical compositions comprising a polypeptide; for the treatment or prevention of diseases needing the increase of a human IFNgamma-related activity; for the treatment or prevention of a disease associated to the excessive human IFNgamma-related activity; for the treatment or prevention of diseases related to a polypeptide; for screening candidate compounds effective to treat a disease related to a polypeptide; method for determining the activity and/or the presence of the polypeptide; or for determining the presence or the amount of a transcript or of a nucleic acid encoding the polypeptide, wherein said polypeptide is:

- a) an isolated polypeptide presenting at least one activity of human IFNgamma, and comprising a sequence having at least 80% of homology with the complete sequence of pIFNFHcon (SEQ ID NO: 156) and no more than nine non-conservative mutations in the positions corresponding to Ala10, Gly12, Arg26, Ala31, Lys35, Phe47, Gln55, Glu57, Lys63, and Ile75 in pIFNFHcon;
- b) an isolated polypeptide that comprises a sequence having at least 80% of homology with the complete sequence of pIFNFHcon and no non-conservative mutations in the positions corresponding to Ala10, Gly12, Arg26, Ala31, Lys35, Phe47, Gln55, Glu57, Lys63, and Ile75 in pIFNFHcon;
- c) an isolated sequence chosen from pIFNFH15 (SEQ ID NO: 20), pIFNFH32 (SEQ ID NO: 32), and pIFNFH37 (SEQ ID NO: 36);
- d) an isolated polypeptide that comprises a sequence having at least 80% of homology with the complete sequence of pIFNFHcon and one or two non-conservative mutations in the positions corresponding to Ala10, Gly12, Arg26, Ala31, Lys35, Phe47, Gln55, Glu57, Lys63, and Ile75 in pIFNFHcon;
- e) an isolated polypeptide as set forth in d) that comprises a sequence chosen from pIFNFH04 (SEQ ID NO: 6), pIFNFH03 (SEQ ID NO: 4), pIFNFH08 (SEQ ID NO:

- 8), pIFNFH20 (SEQ ID NO: 22), pIFNFH23 (SEQ ID NO: 24), pIFNFH12 (SEQ ID NO: 14), pIFNFH25 (SEQ ID NO: 26), pIFNFH13 (SEQ ID NO: 16), pIFNFH14 (SEQ ID NO: 18), pIFNFH36 (SEQ ID NO: 34), and pIFNFH39 (SEQ ID NO: 38);
- f) an isolated polypeptide that comprises a sequence having at least 80% of homology with the complete sequence of pIFNFHcon and three, four, or five non-conservative mutations in the positions corresponding to Ala10, Gly12, Arg26, Ala31, Lys35, Phe47, Gln55, Glu57, Lys63, and Ile75 in pIFNFHcon;
 - g) an isolated polypeptide as set forth in f) that comprises a sequence chosen from pIFNFH11 (SEQ ID NO: 12), pIFNFH27 (SEQ ID NO: 28), pIFNFH01 (SEQ ID NO: 2), pIFNFH31 (SEQ ID NO: 30), pIFNFH10 (SEQ ID NO: 10), and pIFNFH42 (SEQ ID NO: 40);
 - h) an isolated polypeptide that is a variant, a mature form, or an active fragment of the amino acid sequences SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, and 40;
 - i) an isolated polypeptide that is a naturally occurring allelic variant of the sequences SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, and 40;
 - j) an isolated polypeptide as set forth in i), wherein the variant is the translation of one or more single nucleotide polymorphisms; or
 - k) a fusion protein comprising a polypeptide according any one of (a) through (j) and a sequence heterologous to pIFNFHcon.

58 (new). The method according to claim 57, wherein said method for producing cells capable of expressing said polypeptide comprises genetically engineering cells with a vector or a nucleic acid encoding said polypeptide.

59 (new). The method according to claim 57, wherein said method for making a polypeptide comprises culturing a cell under conditions in which a nucleic acid or vector encoding

said polypeptide is expressed and recovering the polypeptide encoded by said nucleic acid or vector from cell culture.

60 (new). The method according to claim 57, wherein said method of treating or preventing a disease when the increase of a human IFNgamma-related activity of a polypeptide of any of the claims from 1 to 10 is needed comprises the administration of said polypeptide, a peptide mimetic or a compound that increases the activity of human IFNgamma-related polypeptide.

61 (new). The method according to claim 57, wherein said method for the treatment or prevention of diseases needing the increase of a human IFNgamma-related activity of a polypeptide comprises the administration of a therapeutically effective amount of said polypeptide, a peptide mimetic, or a compound that increases the activity of a human IFNgamma-related polypeptide.

62 (new). The method according to claim 57, wherein said method for the treatment or prevention of diseases associated to the excessive human IFNgamma-related activity of a comprises the administration of a composition comprising a therapeutically effective amount of a ligand or of a compound.

63 (new). The method according to claim 57, wherein said method for screening candidate compounds effective to treat a disease related to said polypeptide comprises:

- a) contacting a cell or a transgenic non-human organism having enhanced or reduced expression levels of the polypeptide with a candidate compound; and
- b) determining the effect of the compound on the animal or on the cell.

64 (new). The method according to claim 57, said method for identifying a candidate compound as an antagonist/inhibitor or agonist/activator of said polypeptide comprises:

- (a) contacting said polypeptide and said compound with a mammalian cell or a mammalian cell membrane capable of binding the polypeptide; and
- (b) measuring whether the compound blocks or enhances the interaction of the

polypeptide, or the response that results from such interaction, with the mammalian cell or the mammalian cell membrane.

65 (new). The method according to claim 57, wherein said method for determining the activity and/or the presence of said polypeptide of in a sample comprises:

- (a) providing a protein-containing sample;
- (b) contacting said sample with a ligand of; and
- (c) determining the presence of said ligand bound to said polypeptide.

66 (new). The method according to claim 57, wherein said method for determining the presence or the amount of a transcript or of a nucleic acid encoding said polypeptide in a sample comprises:

- (a) providing a nucleic acids-containing sample;
- (b) contacting said sample with a nucleic acid; and
- (c) determining the presence or amount of a transcript or of a nucleic acid encoding said polypeptide.

67 (new). The method according to claim 66, wherein said nucleic acid comprises any of the sequences SEQ ID NOs: 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, or 78.

68 (new). The method according to claim 66, wherein said determining comprises polymerase chain reaction, nucleic acid sequencing, or nucleic acid hybridization.

69 (new). A method of secreting a polypeptide comprising transforming a cell with a nucleic acid encoding a polypeptide comprising pIFNFH01 (SEQ ID NO: 2), pIFNFH03 (SEQ ID NO: 4), pIFNFH04 (SEQ ID NO: 6), pIFNFH08 (SEQ ID NO: 8), pIFNFH10 (SEQ ID NO: 10), pIFNFH11 (SEQ ID NO: 12), pIFNFH12 (SEQ ID NO: 14), pIFNFH13 (SEQ ID NO: 16), pIFNFH14 (SEQ ID NO: 18), pIFNFH15 (SEQ ID NO: 20), pIFNFH20 (SEQ ID NO: 22),

pIFNFH23 (SEQ ID NO: 24), pIFNFH25 (SEQ ID NO: 26), pIFNFH27 (SEQ ID NO: 28), pIFNFH31 (SEQ ID NO: 30), pIFNFH32 (SEQ ID NO: 32), pIFNFH36 (SEQ ID NO: 34), pIFNFH37 (SEQ ID NO: 36), pIFNFH39 (SEQ ID NO: 38), or pIFNFH42 (SEQ ID NO: 40) fused to a heterologous polypeptide.

70 (new). The method according to claim 69, wherein said nucleic acid is chosen from pIFNFH27 (SEQ ID NO: 28), pIFNFH39 (SEQ ID NO: 38), and pIFNFH42 (SEQ ID NO: 40), or any secreted fragment thereof.